

WHAT IS CLAIMED IS:

1. A composition comprising a mutant IgG molecule having an increased serum  
5 half-life relative to IgG, and wherein said mutant IgG molecule has at least one amino  
acid substitution in the Fc-hinge region.
2. The composition of claim 1, wherein said IgG is a human IgG.  
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3. A composition comprising a mutant IgG Fc-hinge fragment having an increased  
serum half-life relative to the serum half-life of IgG, and wherein said fragment has an  
increased binding affinity for FcRn.  
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4. A composition comprising a mutant IgG Fc-hinge fragment having an increased  
serum half-life relative to the serum half-life of IgG, and wherein said fragment has the  
same or slightly lower affinity than IgG for binding to FcRn.  
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5. The composition of claim 1 or claim 3, wherein said molecule or fragment has an amino acid substitution at one or more of the amino acids selected from number 252, 254, 256, 309, 311 or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

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6. The composition of claim 5, wherein said molecule or fragment has three amino acid substitutions at amino acid number 252, 254, 256, 309, 311 or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

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7. The composition of claim 6, wherein said molecule or fragment has the following amino acid substitutions: leucine for threonine at position 252, serine for threonine at position 254 and phenylalanine for threonine at position 256.

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8. The composition of claim 1 or claim 3, wherein said molecule or fragment has a dissociation constant for binding to FcRn at pH 6, of less than about 7 nM as measured by surface plasmon resonance analysis.

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9. The composition of claim 1 or claim 3 further defined as a pharmaceutically acceptable composition.

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10. The composition of claim 5, wherein said amino acid substitutions are generated by random mutagenesis.

11. A method of increasing the serum half-life of an agent comprising conjugating  
said agent to a mutant IgG or IgG Fc hinge fragment having an increased serum half life  
5 of claim 1 or 3.

12. The method of claim 11, wherein said agent is a therapeutic drug.

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13. The method of claim 11, wherein said agent is an antigen binding polypeptide.

14. The method of claim 11, wherein said agent is an antigen or a receptor binding  
15 ligand.

15. The method of claim 14, wherein said receptor binding ligand is a T-cell receptor  
binding ligand.

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16. A method of making an antibody with an increased serum half life comprising;  
  
identifying a first amino acid in an IgG hinge region that is suspected of being  
25 directly involved in FcRn binding;

identifying one or more second amino acids wherein each of said second amino acids is in the spatial region of said first amino acid, and wherein the side chain of said second amino acid is exposed to solvent in the native antibody;

5 making an antibody with a random amino acid substitution of one or more of said second amino acids to make a mutant antibody; and

identifying a mutant antibody having an increased serum half life.

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17. The method of claim 16, further comprising the step of isolating said antibody.

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18. The method of claim 16, wherein said first amino acid is amino acid number 253, 310, 435 or 436 of the Fc fragment.

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19. The method of claim 16, wherein said second amino acid is amino acid number 252, 254, 256, 309, 311 or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

20. The method of claim 16, wherein two or more of said second amino acids are mutated in a single mutant antibody.

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21. An antibody having an increased serum half life, wherein said antibody is made by the method of claim 16.

22. A composition comprising an Fc fragment comprising the fragment from about amino acid 250 to about amino acid 440 of an IgG antibody, further defined as:

5 having a higher binding affinity for FcRn than said IgG antibody;

having one or more amino acid substitutions in a region near one or more FcRn binding amino acid residues; and

10 having a higher binding affinity for FcRn at pH 6 than at pH 7.4.

23. A method of decreasing endogenous serum IgG in a subject comprising administering to said subject an effective amount of the composition of claim 22.

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24. A method of screening an agent for an increased serum half-life relative to the serum half-life of IgG, comprising the steps of:

20 obtaining a candidate agent;

measuring the binding affinity of said agent to FcRn at pH 7.4 and at about pH 6;

25 selecting a candidate agent with a higher binding affinity for FcRn at about pH 6 than at pH 7.4; and

comparing the binding affinity of said selected agent to FcRn to the binding affinity of IgG to FcRn under identical conditions;

wherein an increased binding affinity for FcRn relative to the binding affinity of IgG is indicative of an agent with an increased serum half-life.

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25. The method of claim 24, wherein said candidate agent is a peptide or polypeptide.

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26. The method of claim 25, wherein said peptide or polypeptide is an antibody or a fragment of an antibody.

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27. The method of claim 25, wherein said peptide is selected from a random peptide library.

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28. The method of claim 25, wherein said polypeptide is a protein.

29. The method of claim 28, wherein said protein is a randomly mutated protein.

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30. The method of claim 25, wherein said peptide is a synthetic peptide.

31. The method of claim 25, wherein said peptide is a chemical compound isolated from a random library of synthetic chemical compounds.

32. A method of increasing maternofetal transfer of either antibodies or drugs or proteins or other therapeutic agents comprising administering to said subject an effective amount of the composition of claim 22.

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33. A method of increasing the serum half-life of a therapeutic agent comprising:

conjugating said therapeutic agent to an agent having an increased serum half-life  
10 relative to the serum half-life of IgG identified by the method of claim 23.